REMARKS

Claims 1-18 are pending in the instant application, and all of the pending claims are rejected. Applicants herein cancel claims 3, 6, 9 and 12 without prejudice. As such, upon entry of the instant Amendment and Response, claims 1-2, 4-5, 7-8, 10-11 and 13-18 will be pending.

Regarding priority

The Examiner says that Applicants must provide a certified copy of the priority document and an English translation of the same in order to be afforded the benefit of earlier filed applications thereby overcoming any prior art that arises between the priority date and the actual filing date in the United States.

Applicants respectfully submit that following conversations with WIPO, it is believed that this request is not correct. The present application is a PCT application entering national phase to which specific provisions other than those relating to direct US national filings, apply. Where a PCT application enters the national phase (and as distinct from direct national applications) the overall structure of Article 27 and Rule 51bis—of "the national law applicable by the designated office may require"—shows the hierarchy of the Treaty over the national law/practice, with the Treaty allowing a national Office to require certain specific things in respect of a PCT national phase filing, but clearly defining very narrowly those instances.

Rule 51bis.1(e) allows the national Office to require furnishing of a translation of the priority document, but provided that such a translation may only be required where the validity of the priority claim is relevant to the determination of whether the invention concerned is patentable.

As to any certification of documents, the only instance in which the PCT currently permits the national law to require that certain documents be certified or verified is Rule 51bis.1(d) (that is, the national phase translation).

The applicant may not be required to furnish to the national office a certified copy of the PCT application. The International Bureau communicates to the national Offices concerned a copy of the published application in accordance with PCT Article 20 and Rules 47.1 and 93bis, as has been done in the present case. The copy communicated is a simple

copy, which under the PCT, as explained above, is sufficient for the national phase processing.

Concerning the priority document, Rule 17.2 specifically states that where the applicant has timely furnished the priority document to the International bureau, that bureau furnishes a copy of the priority document to the designated Office upon the specific request of that Office. No such Office will ask the applicant himself to furnish it with a copy (be it simple or certified).

In view of the foregoing, Applicants enclose herewith a sworn translation of the priority document, and respectfully submit that the claimed priority date of July 20, 2001, is perfected.

Regarding the Information Disclosure Statement

The Examiner says that Applicants must provide a brief explanation of the relevance of the listed patents that are not in the English language. Having reviewed the documents filed, Applicants note three applications in Spanish language as follows:

1. Spanish patent application no. 9502361;
2. Certificate of Addition no. 9602522 (an addition to the above application); and
3. PCT application no. WO 97/19938 (claiming priority from both above cited-documents).

Applicants therefore enclose a translation of the corresponding PCT application herewith. Having fulfilled the requirements, Applicants request that the information disclosed in this document be considered with respect to the present application.

Objections to the Claims

The Examiner says that Claim 1 is confusing and unclear. The Examiner suggests an acceptable format. There appear to be misspelled terms in claims 4-6. The Examiner says that claims 3, 6, 9, 12 and 15-16 fail to further limit the claims from which they depend. These claims are herein amended, and it is submitted that they now overcome these objections. Claim 1 has been rewritten to enhance clarity, these modifications being described in detail below. Claim 2 has been amended, introducing the feature concerning conservation of microtubules in liquid nitrogen, support for which may be found in paragraphs 12 and 30 of the specification. In claims 4-6, the misspelling in names of the

compounds have been corrected according to the Examiner's instructions. Claim 3 has been cancelled as its technical features were the same as those disclosed in claim 2. Claims 6, 9, and 12 have also been cancelled as they were dependent on claim 3. Claims 15 and 16 have been amended. The Examiner objected to these claims considering they do not further limit the content of claims 13 and 14 from which they respectively depend. Applicants respectfully submit that these claims refer to determining the quantity of antitumor compounds, whereas claims 13 and 14 refer to the identification of said compounds. These claims have been rephrased to enhance clarity, and support for these claims may be found in paragraphs 10 and 13 of the specification.

Rejection under 35 U.S.C. 102

Claims 1-18 are allegedly anticipated by Diaz *et al., J. Biol. Chem. 2000; 275:26265-26276.* Likewise, claims 1-18 are allegedly anticipated by Andreau, *et al., Biochemistry 2001; 40:11975-11984.* Andreau, *et al.* is not prior art once the claim to priority is perfected.

Applicants submit that having established that the applicable priority date is July 20, 2001 (as explained, supra), it is no longer necessary to consider Andreau et al. as the reference is simply not prior art to the present application. Therefore, it is necessary to address the merits of only Diaz et al. (J. Biol. Chem. 2000; 275: 26265-26276). The Examiner's attention is directed to the present claim 1 that is herein amended, so the second step of the claimed method refers to:

"-determining the displacement equilibrium curve of the probe from the target by any test substance, wherein the biomimetic compound is identified by means of measuring the drop in anisotropy at varying test substance concentrations, or the variation of fluorescence intensity of the probe, or the resonance energy transfer from the probe to a bound acceptor".

This amendment is supported by paragraphs [0013], [0014] and [0026], and Figure 2 of the specification.

Diaz et al. teach that the change in anisotropy was used to measure the binding kinetic and equilibrium constants of Flutax-2, and fluorescence intensity was used to ascertain that this reversibly bound fluorescent probe was displaced by the addition of a large excess of a closely related non-fluorescent competitor, i.e. docetaxel (page 26267, 1st column). However, Diaz et al. do not teach or suggest how to detect a small amount of any chemically

unrelated paclitaxel biomimetic in a problem solution by anisotropy, nor a method to determine the binding constant of a competitor by following the competitor induced Flutax displacement at equilibrium, exemplified in Figure 2 of the specification. Hence, the method recited in claim 1 is neither taught nor suggested by Diaz et al. One of ordinary skill in the art would not assume that the fact that a high excess of docetaxel, a molecule closely related to paclitaxel, displaces Flutax-2 from its binding site on microtubules, is indicative that a displacement curve can be detected, and measured by anisotropy, for substances of unknown binding properties. In fact, the specification teaches the binding of Baccatine III, a compound previously considered as inactive in this context as described in paragraph [0022] of the specification.

Regarding claim 2, Applicants submit that the features concerning the microtubules used in the present invention are novel and were not described in Diaz et al. The microtubules of the present invention have been assembled *in vitro* by the method described, however, their long-term preservation was not. Applicants direct the Examiner's attention to paragraph [0012] and the last two points of paragraph [0030] of the instant specification, where the novel step of dyalisis against a conservation and cryopreservation buffer is disclosed. This step allows the microtubules to be preserved indefinitely frozen in liquid nitrogen until their use. The microtubules obtained by the process described by Diaz et al. are stable only for a few hours at the temperature necessary for the test, rendering them not susceptible of being used in large scale tests. In view of the foregoing, it is apparent that claim 2 is both novel and inventive, and the rejection under 35 U.S.C. 102 is hereby obviated.

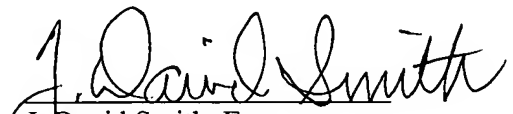
FEES

No additional fees are believed necessary in connection with the present submission; however, should this be in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment or to credit any overage.

CONCLUSION

It is believed that the claims are now in condition for allowance and early notification as such is solicited. If any issues may be resolved by way of a telephone call, the Examiner is invited to call the undersigned at the number indicated below.

Respectfully submitted,



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